DRAFT TOXICOLOGICAL PROFILE FOR AMERICIUM

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

July 2001

AMERICIUM

DISCLAIMER

The use of company or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

AMERICIUM iii

UPDATE STATEMENT

Toxicological profiles are revised and republished as necessary, but no less than once every three years. For information regarding the update status of previously released profiles, contact ATSDR at:

Agency for Toxic Substances and Disease Registry Division of Toxicology/Toxicology Information Branch 1600 Clifton Road NE, E-29 Atlanta, Georgia 30333

AMERICIUM

FOREWORD

This toxicological profile is prepared in accordance with guidelines developed by the Agency for Toxic Substances and Disease Registry (ATSDR) and the Environmental Protection Agency (EPA). The original guidelines were published in the *Federal Register* on April 17, 1987. Each profile will be revised and republished as necessary.

The ATSDR toxicological profile succinctly characterizes the toxicologic and adverse health effects information for the hazardous substance described therein. Each peer-reviewed profile identifies and reviews the key literature that describes a hazardous substance's toxicologic properties. Other pertinent literature is also presented, but is described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

The focus of the profiles is on health and toxicologic information; therefore, each toxicological profile begins with a public health statement that describes, in nontechnical language, a substance's relevant toxicological properties. Following the public health statement is information concerning levels of significant human exposure and, where known, significant health effects. The adequacy of information to determine a substance's health effects is described in a health effects summary. Data needs that are of significance to protection of public health are identified by ATSDR and EPA.

Each profile includes the following:

- (A) The examination, summary, and interpretation of available toxicologic information and epidemiologic evaluations on a hazardous substance to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects;
- (B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure that present a significant risk to human health of acute, subacute, and chronic health effects; and
- (C) Where appropriate, identification of toxicologic testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

The principal audiences for the toxicological profiles are health professionals at the Federal, State, and local levels; interested private sector organizations and groups; and members of the public. We plan to revise these documents in response to public comments and as additional data become available. Therefore, we encourage comments that will make the toxicological profile series of the greatest use.

Comments should be sent to:

Agency for Toxic Substances and Disease Registry Division of Toxicology 1600 Clifton Road, N.E. Mail Stop E-29 Atlanta, Georgia 30333

Background Information

The toxicological profiles are developed by ATSDR pursuant to Section 104(i) (3) and (5) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund) for hazardous substances found at Department of Energy (DOE) waste sites. CERCLA directs ATSDR to prepare toxicological profiles for hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL) and that pose the most significant potential threat to human health, as determined by ATSDR and the EPA. ATSDR and DOE entered into a Memorandum of Understanding on November 4, 1992 which provided that ATSDR would prepare toxicological profiles for hazardous substances based upon ATSDR's or DOE's identification of need. The current ATSDR priority list of hazardous substances at DOE NPL sites was announced in the Federal Register on July 24, 1996 (61 FR 38451).

This profile reflects ATSDR's assessment of all relevant toxicologic testing and information that has been peer-reviewed. Staff of the Centers for Disease Control and Prevention and other Federal scientists have also reviewed the profile. In addition, this profile has been peer-reviewed by a nongovernmental panel and is being made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

Jeffrey P. Koplan, M.D., M.P.H.

Administrator

Agency for Toxic Substances and Disease Registry

AMERICIUM vii

QUICK REFERENCE FOR HEALTH CARE PROVIDERS

Toxicological Profiles are a unique compilation of toxicological information on a given hazardous substance. Each profile reflects a comprehensive and extensive evaluation, summary, and interpretation of available toxicologic and epidemiologic information on a substance. Health care providers treating patients potentially exposed to hazardous substances will find the following information helpful for fast answers to often-asked questions.

Primary Chapters/Sections of Interest

- **Chapter 1: Public Health Statement**: The Public Health Statement can be a useful tool for educating patients about possible exposure to a hazardous substance. It explains a substance's relevant toxicologic properties in a nontechnical, question-and-answer format, and it includes a review of the general health effects observed following exposure.
- **Chapter 2: Relevance to Public Health**: The Relevance to Public Health Section evaluates, interprets, and assesses the significance of toxicity data to human health.
- **Chapter 3: Health Effects**: Specific health effects of a given hazardous compound are reported by *type of health effect* (death, systemic, immunologic, reproductive), by *route of exposure*, and by *length of exposure* (acute, intermediate, and chronic). In addition, both human and animal studies are reported in this section.

NOTE: Not all health effects reported in this section are necessarily observed in the clinical setting. Please refer to the Public Health Statement to identify general health effects observed following exposure.

Pediatrics: Four new sections have been added to each Toxicological Profile to address child health issues:

Section 1.7 How Can (Chemical X) Affect Children?

Section 1.8 How Can Families Reduce the Risk of Exposure to (Chemical X)?

Section 3.7 Children's Susceptibility

Section 6.6 Exposures of Children

Other Sections of Interest:

Section 3.8 Biomarkers of Exposure and Effect

Section 3.11 Methods for Reducing Toxic Effects

ATSDR Information Center

Phone: 1-888-42-ATSDR or (404) 498-0110 **Fax:** (404) 498-0057

The following additional material can be ordered through the ATSDR Information Center:

Case Studies in Environmental Medicine: Taking an Exposure History—The importance of taking an exposure history and how to conduct one are described, and an example of a thorough exposure history is provided. Other case studies of interest include Reproductive and Developmental Hazards; Skin Lesions and Environmental Exposures; Cholinesterase-Inhibiting Pesticide Toxicity; and numerous chemical-specific case studies.

AMERICIUM viii

Managing Hazardous Materials Incidents is a three-volume set of recommendations for on-scene (prehospital) and hospital medical management of patients exposed during a hazardous materials incident. Volumes I and II are planning guides to assist first responders and hospital emergency department personnel in planning for incidents that involve hazardous materials. Volume III—Medical Management Guidelines for Acute Chemical Exposures—is a guide for health care professionals treating patients exposed to hazardous materials.

Fact Sheets (ToxFAQs) provide answers to frequently asked questions about toxic substances.

Other Agencies and Organizations

- The National Center for Environmental Health (NCEH) focuses on preventing or controlling disease, injury, and disability related to the interactions between people and their environment outside the workplace. Contact: NCEH, Mailstop F-29, 4770 Buford Highway, NE, Atlanta, GA 30341-3724 Phone: 770-488-7000 FAX: 770-488-7015.
- The National Institute for Occupational Safety and Health (NIOSH) conducts research on occupational diseases and injuries, responds to requests for assistance by investigating problems of health and safety in the workplace, recommends standards to the Occupational Safety and Health Administration (OSHA) and the Mine Safety and Health Administration (MSHA), and trains professionals in occupational safety and health. Contact: NIOSH, 200 Independence Avenue, SW, Washington, DC 20201 Phone: 800-356-4674 or NIOSH Technical Information Branch, Robert A. Taft Laboratory, Mailstop C-19, 4676 Columbia Parkway, Cincinnati, OH 45226-1998 Phone: 800-35-NIOSH.
- The National Institute of Environmental Health Sciences (NIEHS) is the principal federal agency for biomedical research on the effects of chemical, physical, and biologic environmental agents on human health and well-being. Contact: NIEHS, PO Box 12233, 104 T.W. Alexander Drive, Research Triangle Park, NC 27709 Phone: 919-541-3212.
- Radiation Emergency Assistance Center/Training Site (REAC/TS) provides support to the U.S.

 Department of Energy, the World Health Organization, and the International Atomic Energy Agency in the medical management of radiation accidents. A 24-hour emergency response program at the Oak Ridge Institute for Science and Education (ORISE), REAC/TS trains, consults, or assists in the response to all kinds of radiation accidents. Contact: Oak Ridge Institute for Science and Education, REAC/TS, PO Box 117, MS 39, Oak Ridge, TN 37831-0117

 Phone 865-576-3131 FAX 865-576-9522 24-Hour Emergency Phone 865-576-1005 (ask for REAC/TS) e-mail: cooleyp@orau.gov website (including emergency medical guidance): http://www.orau.gov/reacts/default.htm

Referrals

The Association of Occupational and Environmental Clinics (AOEC) has developed a network of clinics in the United States to provide expertise in occupational and environmental issues. Contact:

 AOEC, 1010 Vermont Avenue, NW, #513, Washington, DC 20005 • Phone: 202-347-4976
 • FAX: 202-347-4950 • e-mail: aoec@dgs.dgsys.com
 • AOEC Clinic Director: http://occ-env-med.mc.duke.edu/oem/aoec.htm.

AMERICIUM ix

The American College of Occupational and Environmental Medicine (ACOEM) is an association of physicians and other health care providers specializing in the field of occupational and environmental medicine. Contact: ACOEM, 55 West Seegers Road, Arlington Heights, IL 60005 • Phone: 847-818-1800 • FAX: 847-818-9266.

AMERICIUM x

CONTRIBUTORS

CHEMICAL MANAGER(S)/AUTHORS(S):

Sam Keith, M.S., C.H.P ATSDR, Division of Toxicology, Atlanta, GA

David W. Wohlers, Ph.D Gloria W. Sage, Ph.D. Gary L. Diamond, Ph.D. Michael Neal, Ph.D. Syracuse Research Corporation, North Syracuse, NY

THE PROFILE HAS UNDERGONE THE FOLLOWING ATSDR INTERNAL REVIEWS:

- 1. Health Effects Review. The Health Effects Review Committee examines the health effects chapter of each profile for consistency and accuracy in interpreting health effects and classifying end points.
- 2. Minimal Risk Level Review. The Minimal Risk Level Workgroup considers issues relevant to substance-specific minimal risk levels (MRLs), reviews the health effects database of each profile, and makes recommendations for derivation of MRLs.
- 3. Data Needs Review. The Research Implementation Branch reviews data needs sections to assure consistency across profiles and adherence to instructions in the Guidance.

AMERICIUM xiii

PEER REVIEW

A peer review panel was assembled for americium. The panel consisted of the following members:

- 1. Raymond Guilmette, Ph.D., Manager, Radiation Toxicology Program, Lovelace Respiratory Research Institute, Albuquerque, NM
- 2. Ronald Kathren, C.H.P., D.E.E., Professor of Pharmaceutical Science, Washington State University; President, The Kathren Group, Inc., Richland, WA
- 3. Raymond Lloyd, Ph.D., Professor Emeritus of Radiobiology, University of Utah School of Medicine, Taylorsville, UT
- 4. Melvin Sikov, Ph.D., Scientist Emeritus, Pacific Northwest National Laboratory, Richland, WA

These experts collectively have knowledge of americium's physical and chemical properties, toxico-kinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(I)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

Scientists from the Agency for Toxic Substances and Disease Registry (ATSDR) have reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profile lies with the ATSDR.

AMERICIUM xv

CONTENTS

FOREWORD .	
QUICK REFERE	ENCE FOR HEALTH CARE PROVIDERS
CONTRIBUTOR	S
PEER REVIEW	xii
LIST OF FIGUR	ES xiz
LIST OF TABLE	ESxx
1.1 WHAT 1.2 WHAT 1.3 HOW M 1.4 HOW C 1.5 HOW C 1.6 HOW C 1.7 HOW C 1.8 IS THE AMERI 1.9 WHAT PROTE	IS AMERICIUM? HAPPENS TO AMERICIUM WHEN IT ENTERS THE ENVIRONMENT? MIGHT I BE EXPOSED TO AMERICIUM? CAN AMERICIUM ENTER AND LEAVE MY BODY? CAN AMERICIUM AFFECT MY HEALTH? CAN AMERICIUM AFFECT CHILDREN? CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO AMERICIUM? RE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO ICIUM? RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO ICIUMAN HEALTH? E CAN I GET MORE INFORMATION?
2.1 BACKO UNITE 2.2 SUMM	E TO PUBLIC HEALTH GROUND AND ENVIRONMENTAL EXPOSURES TO AMERICIUM IN THE D STATES ARY OF HEALTH EFFECTS (AL RISK LEVELS 12
3.1 INTRO 3.2 DISCU	FECTS 15 DUCTION 15 SSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE 16 Inhalation Exposure 17 3.2.1.1 Death 17 3.2.1.2 Systemic Effects 18 3.2.1.3 Immunological and Lymphoreticular Effects 25 3.2.1.4 Neurological Effects 27 3.2.1.5 Reproductive Effects 27 3.2.1.6 Developmental Effects 27 3.2.1.7 Cancer 27 Oral Exposure 27 3.2.2.1 Death 27 3.2.2.2 Systemic Effects 27 3.2.2.3 Immunological and Lymphoreticular Effects 27

	3.2.2.4	Neurological Effects	. 22
	3.2.2.5	Reproductive Effects	. 22
	3.2.2.6		
3 2 3			
5.2.5			
		·	
		•	
3.2.4	External	Exposure	. 24
	3.2.4.1	Death	. 25
	3.2.4.2		
	3 2 4 3		
2.2.5			
3.2.5			
	3.2.5.3		
	3.2.5.4	Neurological Effects	. 26
	3.2.5.5	Reproductive Effects	. 27
	3.2.5.6	Developmental Effects	. 27
	3.2.5.7		
GENOT			
J. T .1			
		•	
3.4.2			
		*	
	3.4.2.2	Oral Exposure	. 45
	3.4.2.3	Dermal Exposure	. 45
	3.4.2.4	Other Routes of Exposure	. 46
3.4.3	Metaboli	sm	. 47
		<u>*</u>	
3 1 1			
3.7.7			
			. 50
3.4.5		• • • • • • • • • • • • • • • • • • • •	
	Models .		. 51
	3.2.5 GENOT TOXIC 3.4.1	3.2.2.5 3.2.2.6 3.2.2.7 3.2.3 Dermal E 3.2.3.1 3.2.3.2 3.2.3.3 3.2.3.4 3.2.3.5 3.2.3.6 3.2.3.7 3.2.4 External 3.2.4.1 3.2.4.2 3.2.4.3 3.2.4.4 3.2.4.5 3.2.4.6 3.2.4.7 3.2.5 Other Ro 3.2.5.1 3.2.5.2 3.2.5.3 3.2.5.4 3.2.5.5 3.2.5.6 3.2.5.7 GENOTOXICITY TOXICOKINETIC 3.4.1 Absorptic 3.4.1.1 3.4.1.2 3.4.1.3 3.4.1.4 3.4.2 3.4.3.3 3.4.2.4 3.4.3 3.4.3.3 3.4.4.4 3.4.3 3.4.4.4 3.4.5 Physiolog 3.4.3.3 3.4.4.4 3.4.5 Physiolog 3.4.3.3 3.4.4.4 3.4.5 Physiolog 3.4.3.3 3.4.4.4 3.4.5 Physiolog 3.4.3.3 3.4.4.4	3.2.5 Reproductive Effects 3.2.6 Developmental Effects 3.2.7 Cancer 3.2.3 Death 3.2.3.1 Death 3.2.3.2 Systemic Effects 3.2.3.3 Immunological and Lymphoreticular Effects 3.2.3.4 Neurological Effects 3.2.3.5 Reproductive Effects 3.2.3.7 Cancer 3.2.4 Death 3.2.4.2 Systemic Effects 3.2.4.1 Death 3.2.4.2 Systemic Effects 3.2.4.3 Immunological and Lymphoreticular Effects 3.2.4.3 Immunological and Lymphoreticular Effects 3.2.4.5 Reproductive Effects 3.2.5.1 Death 3.2.5.1 Death 3.2.5.2 Systemic Effects 3.2.5.1 Death 3.2.5.3 Immunological and Lymphoreticular Effects 3.2.5.1 Death 3.2.5.2 Systemic Effects 3.2.5.3 Immunological and Lymphoreticular Effects 3.2.5.6 Developmental Effects 3.2.5.6 Developmental Effects 3.2.5.6 Developmental Effects 3.2.5.7 Cancer GENOTOXICITY TOXICOKINETICS 3.4.1.1 Inhalation Exposure 3.4.1.2 Oral Exposure 3.4.1.3 Dermal Exposure 3.4.2.1 Inhalation Exposure 3.4.2.2 Oral Exposure 3.4.2.3 Dermal Exposure 3.4.2.3 Dermal Exposure 3.4.2.3 Dermal Exposure 3.4.2.3 Dermal Exposure 3.4.3.3 Dermal Exposure 3.4.4.4 Other Routes of Exposure 3.4.4.2 Oral Exposure 3.4.3.3 Dermal Exposure 3.4.4.3 Dermal Exposure 3.4.4.3 Dermal Exposure 3.4.4.3 Dermal Exposure 3.4.4.4 Other Routes of Exposure 3.4.4.3 Dermal Exposure 3.4.4.4 Other Routes of Exposure 3.4.4.5 Oral Exposure 3.4.4.6 Oral Exposure 3.4.4.7 Oral Exposure 3.4.4.8 Oral Exposure 3.4.4.9 Oral Exposure 3.4.4.9 Oral Exposure 3.4.4.9 Oral Exposure 3

	3.5	MECHANISMS OF ACTION	77
		3.5.1 Pharmacokinetic Mechanisms	77
		3.5.2 Mechanisms of Toxicity	80
		3.5.3 Animal-to-Human Extrapolations	80
	3.6	ENDOCRINE DISRUPTION	81
	3.7	CHILDREN'S SUSCEPTIBILITY	81
	3.8	BIOMARKERS OF EXPOSURE AND EFFECT	85
		3.8.1 Biomarkers Used to Identify or Quantify Exposure to Americium	86
		3.8.2 Biomarkers Used to Characterize Effects Caused by Americium	
	3.9	INTERACTIONS WITH OTHER CHEMICALS	
	3.10	POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE	
		METHODS FOR REDUCING TOXIC EFFECTS	
		3.11.1 Reducing Peak Absorption Following Exposure	
		3.11.2 Reducing Body Burden	88
		3.11.3 Interfering with the Mechanism of Action for Toxic Effects	89
	3 12	ADEQUACY OF THE DATABASE	
	J.1. <u>-</u>	3.12.1 Existing Information on Health Effects of Americium	
		3.12.2 Identification of Data Needs	
		3.12.3 Ongoing Studies	
		5.12.5 Ongoing Station	,
4	CHEN	MICAL, PHYSICAL, AND RADIOLOGICAL INFORMATION	99
••	4.1	CHEMICAL IDENTITY	
	4.2	PHYSICAL, CHEMICAL, AND RADIOLOGICAL PROPERTIES	
		1111 510112, 01121110112, 11112 1112102001211211111211112	
5.	PROI	DUCTION, IMPORT/EXPORT, USE, AND DISPOSAL	105
	5.1	PRODUCTION	
	5.2	IMPORT/EXPORT	
	5.3	USE	
	5.4	DISPOSAL	
	٠		100
6.	POTE	ENTIAL FOR HUMAN EXPOSURE	109
	6.1	OVERVIEW	
	6.2	RELEASES TO THE ENVIRONMENT	
	٥.ــ	6.2.1 Air	
		6.2.2 Water	
		6.2.3 Soil	
	6.3		118
	0.5		118
			135
		<u> </u>	135
			135
			135
	6.4		136
	0.4		136
			138
			140
			140
	6.5		_
	6.5		155
	6.6		160
	6.7	POPULATIONS WITH POTENTIALLY HIGH EXPOSURES	101

AMERICIUM xviii

	6.8	ADEQUACY OF THE DATABASE	162
		6.8.1 Identification of Data Needs	162
		6.8.2 Ongoing Studies	165
7.	ANA	LYTICAL METHODS	167
	7.1	BIOLOGICAL MATERIALS	167
		7.1.1 Internal Americium Measurements	167
		7.1.2 External Radiation Measurements	172
	7.2	ENVIRONMENTAL SAMPLES	173
		7.2.1 Field Measurements of Americium	173
		7.2.2 Laboratory Analysis of Environmental Samples	
	7.3	ADEQUACY OF THE DATABASE	182
		7.3.1 Identification of Data Needs	
		7.3.2 Ongoing Studies	183
		ULATIONS AND ADVISORIES ERENCES	185 193
10	. GLC	OSSARY	235
ΑF	PENI	DICES	
	A.	ATSDR MINIMAL RISK LEVEL AND WORKSHEETS	A- 1
	B.	USER'S GUIDE	B-1
	C.	ACRONYMS, ABBREVIATIONS, AND SYMBOLS	C-1
	D.	OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY AND BIOLOGY	D-1

AMERICIUM xix

LIST OF FIGURES

3-1.	Conceptual Representation of a Physiologically Based Pharmacokinetic (PBPK) Model for a Hypothetical Chemical Substance	53
3-2.	Respiratory Tract Compartments in Which Particles May be Deposited	55
3-3.	Reaction of Gases or Vapors at Various Levels of the Gas-Blood Interface	60
3-4.	Compartment Model to Represent Time-Dependent Particle Transport in the Respiratory Tract	61
3-5.	The Human Respiratory Tract Model: Absorption into Blood	64
3-6.	ICRP (1989) Model of Americium Biokinetics	66
3-7.	Leggett (1992) Model of Americium Biokinetics	69
3-8.	Leggett (1992) Model of Deposition and Retention of Americium in the Human Respiratory Tract	70
3-9.	Mewhinney and Griffith (1983) Model of Deposition and Retention of Americium in the Human Respiratory Tract	74
3-10.	Durbin and Schmidt (1985) Model of Distribution and Excretion of Absorbed Americium in the Human	
3-11.	Existing Information on Health Effects of Americium	91
6-1.	Frequency of NPL Sites with Americium Contamination	10

AMERICIUM xxi

LIST OF TABLES

J - 1.	Inhalation	31
3-2.	Absorption Estimates in Animals Exposed to Americium Compounds by Ingestion	37
3-3.	Tissue Americium Levels from Human Autopsies	42
3-4.	Reference Respiratory Values for a General Caucasian Population at Different Levels of Activity	. 57
3-5.	Reference Values of Parameters for the Compartment Model to Represent Time-dependent Particle Transport from the Human Respiratory Tract	. 58
4-1.	Principal Americium Isotopes	100
4-2.	Physical and Chemical Properties of Americium and Selected Americium Compounds	102
4-3.	Properties of Some Americium Ions	104
6-1.	Concentrations of Americium 241 in Soil and Sediment	120
6-2.	Bioconcentration Factors for ²⁴¹ Am	132
6-3.	Concentrations of ²⁴¹ Am in Water	139
6-4.	Average Concentrations of ²⁴¹ Am in Food	144
6-5.	Concentrations of ²⁴¹ Am in Fauna	148
6-6.	Estimated Effective ²⁴¹ Am Dose from Food Raised on Land Impacted by Tidal Estuaries along the Irish Sea	157
6-7.	Ongoing Studies on Environmental Effects of Americium	166
7-1.	Analytical Methods for Determining Americium in Biological Samples	168
7-2.	Analytical Methods for Determining Americium in Environmental Samples	176
8-1.	Regulations and Guidelines Applicable to Americium	186